FORMULATIONS FOR EXTENDING LIFESPAN AND HEALTHSPAN

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application No. 62/489,884 filed April 25, 2017; and U.S. Provisional Application No. 62/646,734 filed March 22, 2018, which are incorporated by reference herein in their entirety.

BACKGROUND OF THE INVENTION

[0002] Pharmacological treatment and prevention of the natural declines of age and aging-related diseases has presented challenges to the medical community in part because of the stringent characteristics required of pharmacological agents for this purpose. Aging patient populations impose unusually high burdens on pharmacological therapies to be bioavailable, nontoxic, and lacking long-term adverse effects. Prevention requires treatment of patients which may be at risk to aging-related disorders but experiencing no or mild symptoms, requiring agents that do not damage existing health. Treatment of patients with existing age-related disease requires a high requirement for nontoxicity, so as to not exacerbate existing health conditions. Moreover, treatment or prevention of aging-related disorders in general likely requires treatment with pharmacological agents for many years, thus requiring such agents to lack cumulative toxicity or long-term deleterious effects on organ systems.

[0003] Accordingly, there is a need for discovery of pharmacological agents and combinations of pharmacological agents that are nontoxic and suitable for administration to subjects before age related disorders are apparent or acute, or for the longer-term administration.

[0004] The primary and secondary metabolites present in dietary fruits and vegetables are a chemically diverse pharmacopeia which meets the criteria for treatment of aging related diseases. Due to their longstanding presence in the human diet, many of these compounds have very low toxicity and well-understood pharmacokinetic parameters. Screening of compounds from these sources thus provides great potential for the therapy of aging and aging-related conditions.

SUMMARY OF THE INVENTION

[0004a] In one aspect, disclosed herein are uses of a composition comprising α-ketoglutarate (AKG) and a vitamin D compound in the manufacture of a medicament for delaying onset or delaying progression of frailty.

[0005] Disclosed herein, in certain embodiments, are methods of extending lifespan in a subject in need thereof comprising administering to the subject a therapeutically effective amount of berberine, a vitamin A compound, and α-ketoglutarate (AKG). In some instances, berberine, the vitamin A compound and AKG is administered to the subject as a single composition. In some instances, the berberine, the vitamin A compound, and α-ketoglutarate are administered to the subject separately. In some instances, the berberine, the vitamin A compound, and α-ketoglutarate are administered to the subject within a 24 hour period. In some instances, the vitamin A compound is selected from the group consisting of retinol, retinal, retinoic acid, retinyl palmitate, alpha-carotene, beta-carotene, and gamma-carotene. In some instances, the vitamin A compound is retinoic acid or retinyl palmitate. In some instances, AKG is formulated as a calcium salt. In some instances, the subject is a mammal. In some instances, the mammal is a human. In some instances, the mammal is a dog. In some instances, the mammal is a cat. In some